Supported Chiral Monodentate Ligands in Rhodium-Catalysed Asymmetric Hydrogenation and Palladium-Catalysed Asymmetric Allylic Alkylation

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SUPPORTING INFORMATION

Title: Supported Chiral Monodentate Ligands in Rhodium-Catalysed Asymmetric Hydrogenation and Palladium-Catalysed Asymmetric Allylic Alkylation

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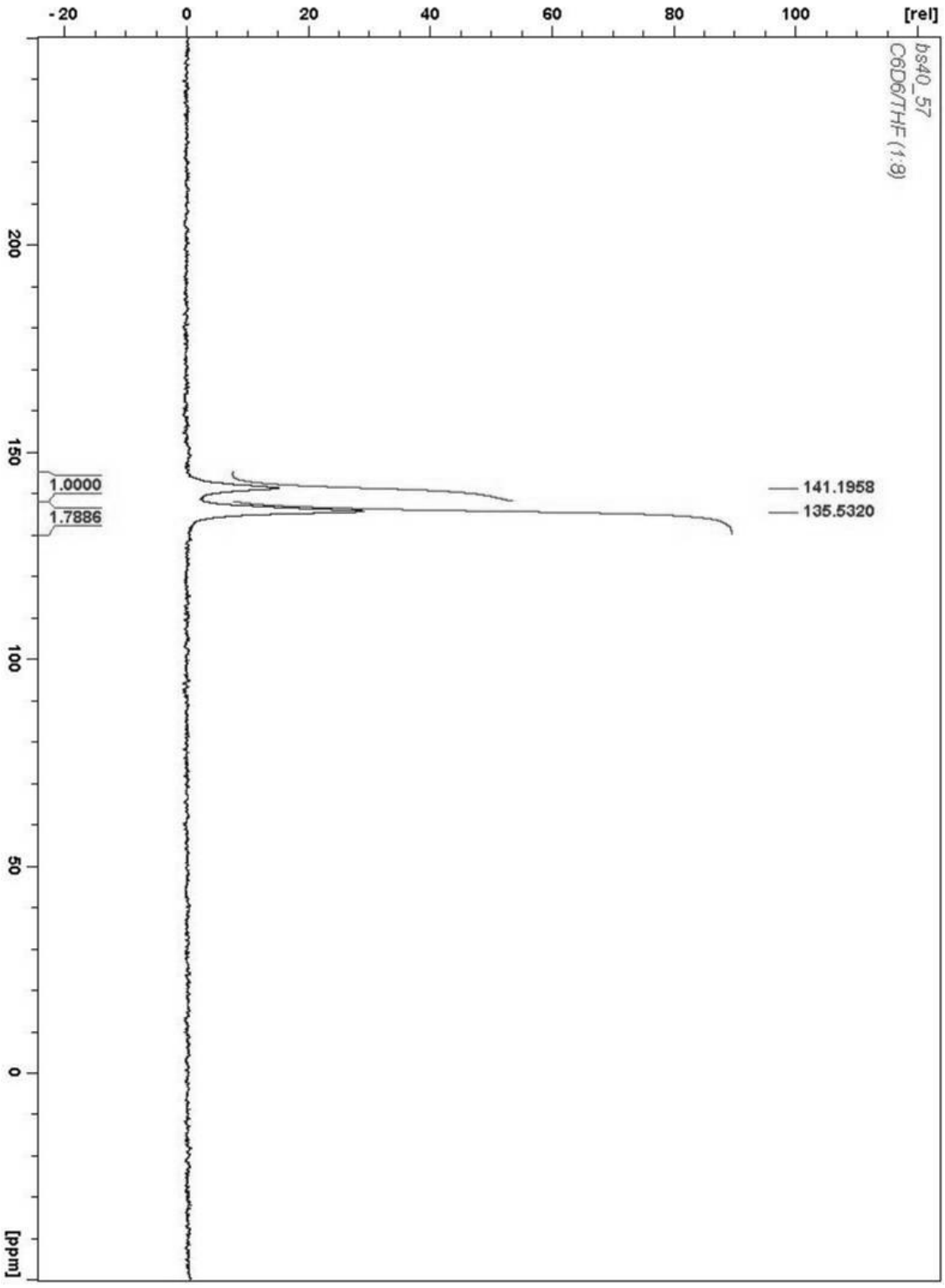
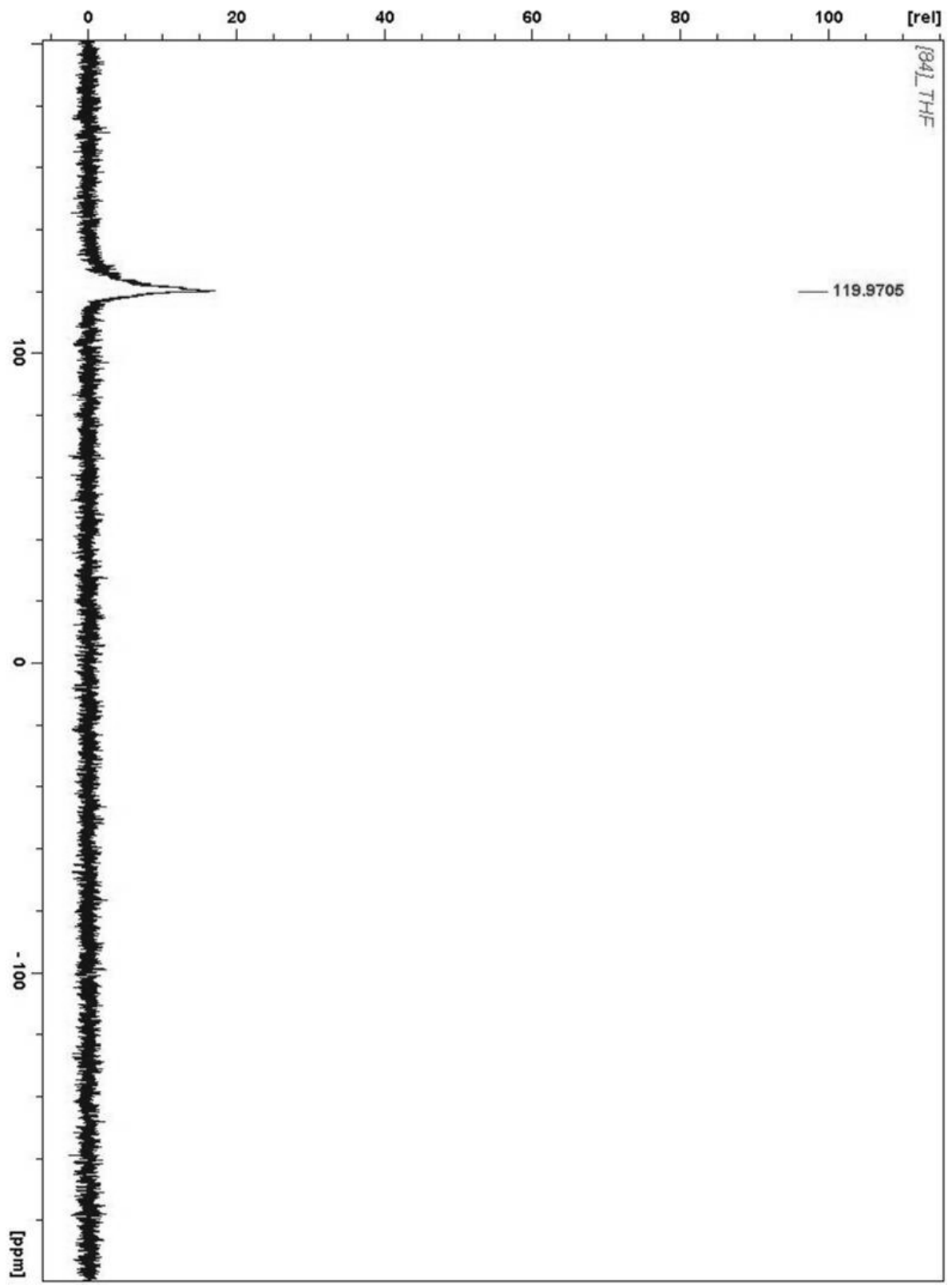
Gel-phase ^{31}P NMR spectrum of **A9**

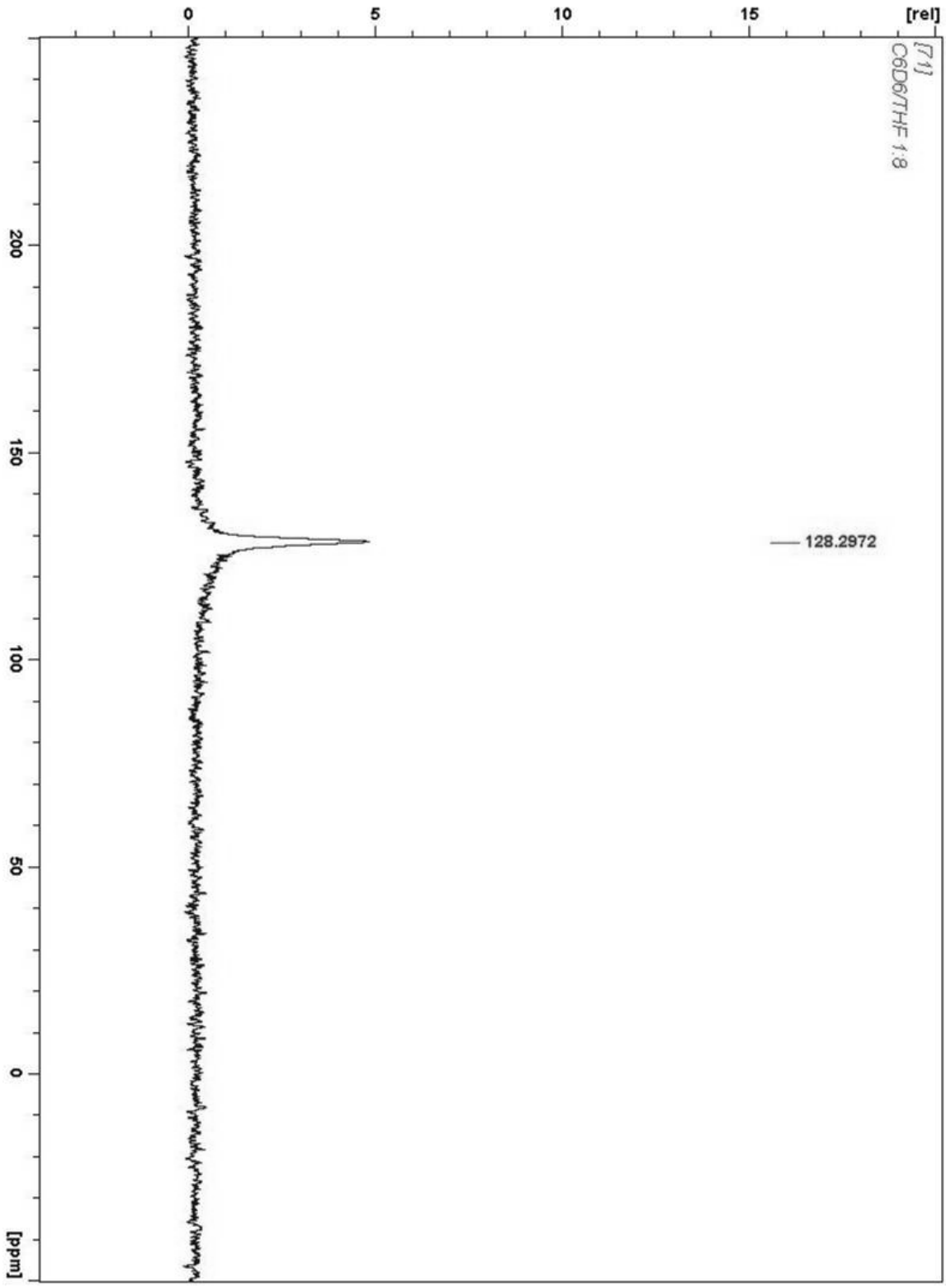
(solvent = THF-C_6D_6 8:1)



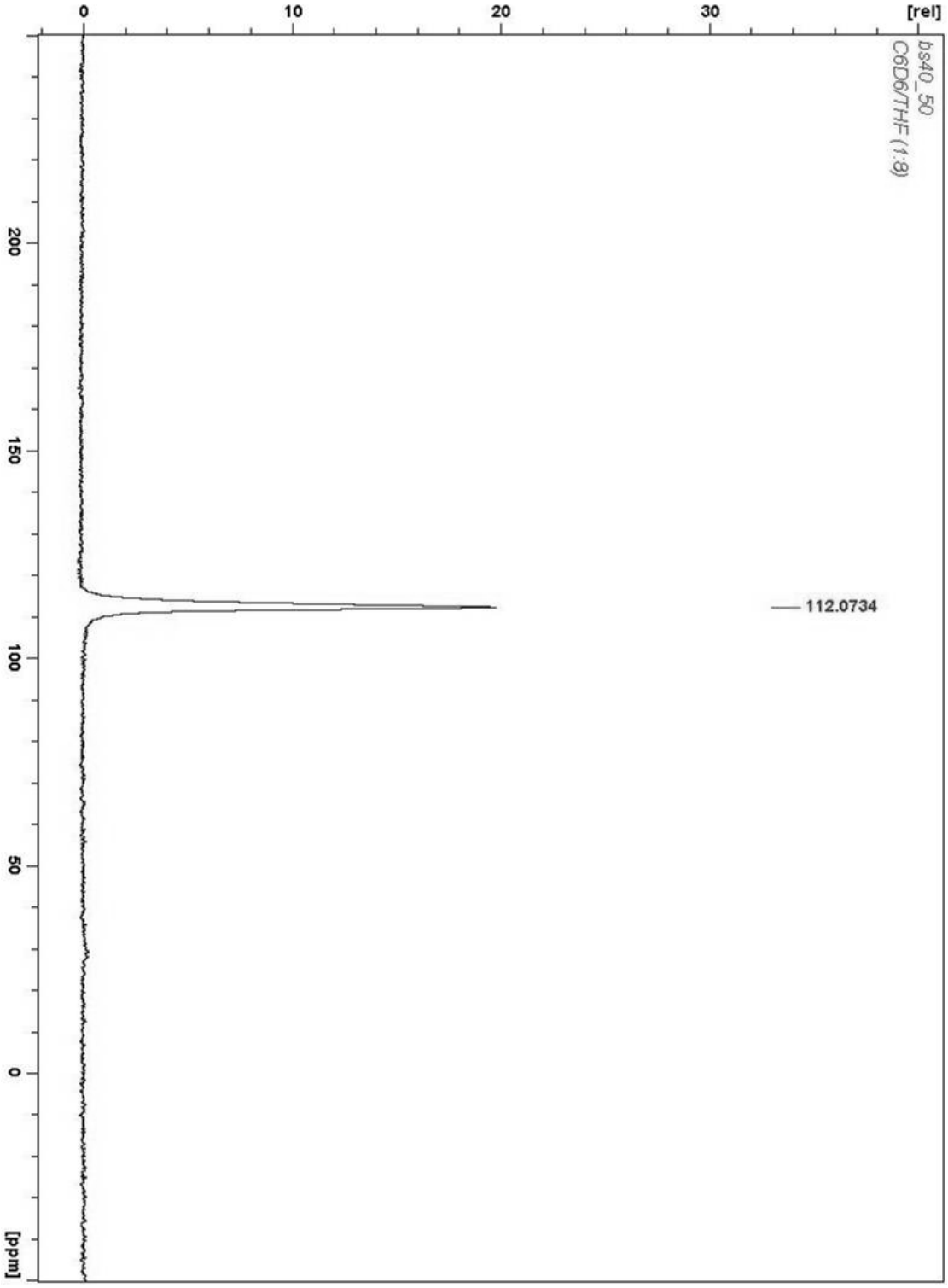
Gel-phase ^{31}P NMR spectrum of **A10**
(solvent = THF)



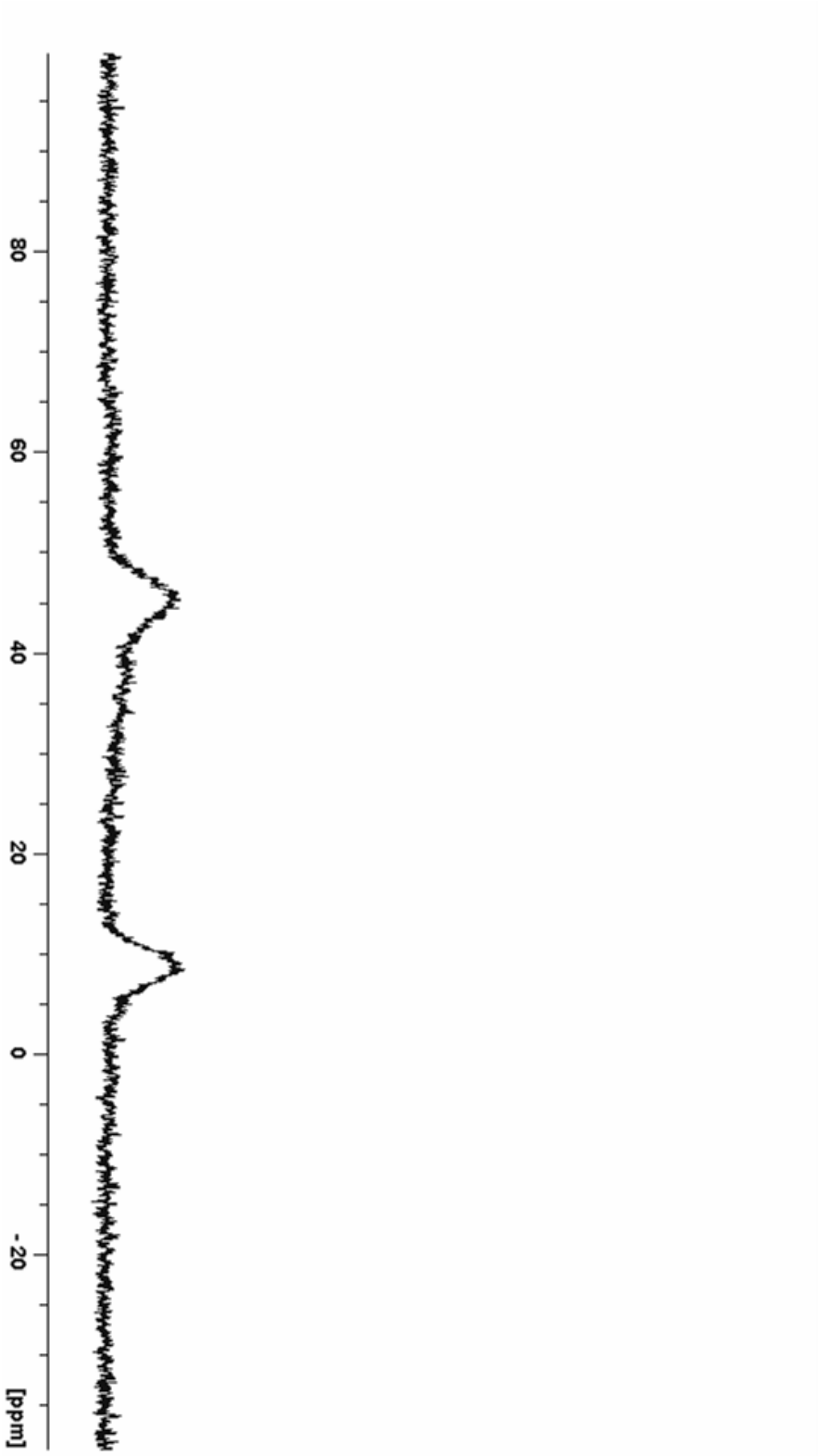
Gel-phase ^{31}P NMR spectrum of **A11**
(solvent = THF-C_6D_6 8:1)



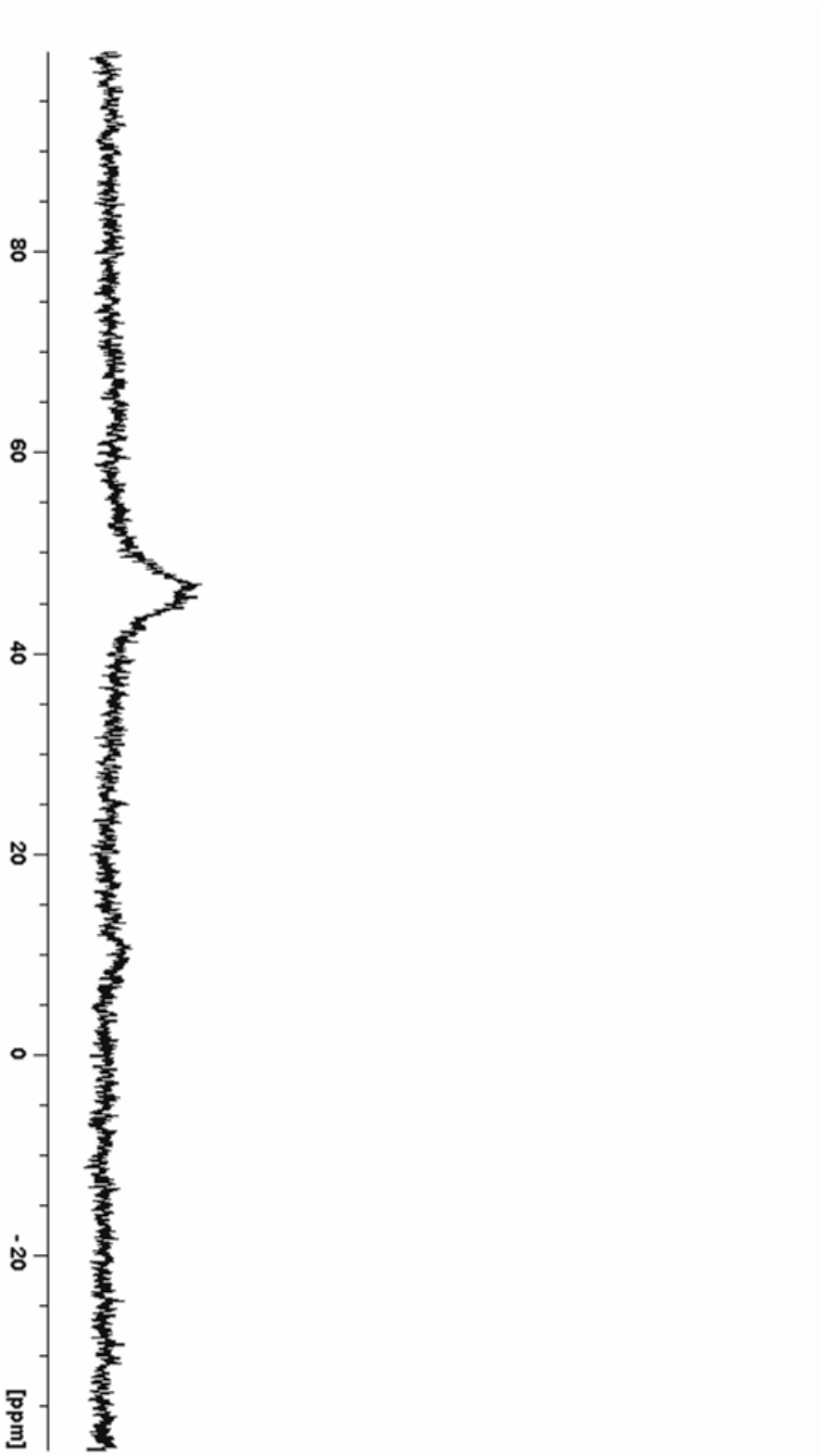
Gel-phase ^{31}P NMR spectrum of **A14**
(solvent = THF-C_6D_6 8:1)



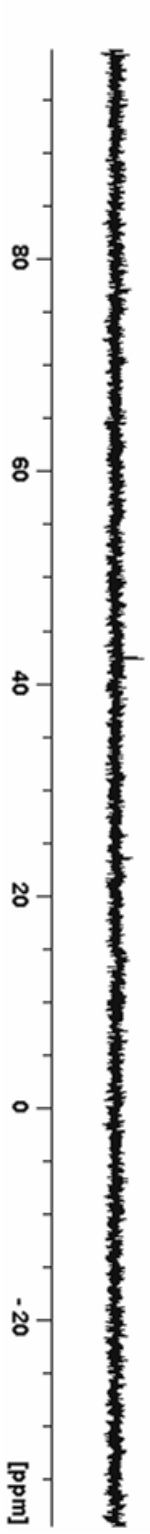
In situ gel-phase ^{31}P NMR spectrum of **F15** + 0.25 equivalent $[Pd(allyl)Cl]_2$
(solvent = THF-C_6D_6 8:1)



In situ gel-phase ^{31}P NMR spectrum of **F15** + 0.5 equivalent $[Pd(allyl)Cl]_2$ + 1 equivalent PPh_3
(solvent = THF-C_6D_6 8:1)



^{31}P NMR spectrum of the THF-C_6D_6 (8:1) phase above resin **F15**, after reaction with 0.5 equivalent $[Pd(allyl)Cl]_2$ and 1 equivalent PPh_3



Catalytic experiments (general procedures)

Allylic substitution: In a Schlenk flask the polymer-supported ligand and KOAC (1 mg) were suspended in DCM. After 15 minutes $[Pd(allyl)Cl]_2$, 1,3-diphenylallyl acetate (**5**, 126 mg, 0.5 mmol), *n*-decane, as internal standard for GC measurements, and if applicable the second phosphorus ligand were added via freshly prepared stock-solutions in DCM. After 15 minutes the reaction was started by addition of 0.085 ml dimethyl malonate (**6**, 0.75 mmol) and 0.185 ml *N, O*-bis(trimethylsilyl)acetamide (BSA, 0.75 mmol). After 16 hours the reaction was stopped by the addition of Et_2O (5 ml) and a saturated aqueous ammonium chloride solution (5 ml). The organic layer was subsequently dried over $MgSO_4$ and an aliquot was analyzed by GC to determine the yield, while the rest was evaporated to dryness, to yield the crude product. This was further purified by flash column chromatography (silica gel 60, particle size 0.063–0.2 mm from Fluka, EtOAc/PE 40-60 1:5) to yield a colorless oil. The enantiomeric excess of the product was determined by chiral HPLC (Daicel OD; n-hexane/2-propanol 99.5:0.5; flow 0.5 ml/min; ν = 254 nm. t_R (*R*–product) = 42.1 min., t_R (*S*–product) = 45.8 min.).

Hydrogenation: The hydrogenation experiments were performed in a stainless steel autoclave (volume 150 ml) equipped with an insert suitable for 10 reaction vessels (including Teflon mini stirring bars) for conducting parallel reactions. The polymer-supported ligand was weighed in a reaction vial and was subsequently brought under an inert atmosphere. He catalyst precursor $[Rh(COD)_2]BF_4$ or $[(COD)Rh(MeCN)_2]BF_4$ and if applicable the second phosphorus ligand were added via freshly prepared stock-solutions in DCM (total volume = 1.8 ml). The supported catalyst was allowed to form for a specific incubation period (e.g. 30 minutes or 16 hours). In situ prepared catalysts were used at this stage. Purification of the catalyst was done by removal of the solution phase using a syringe equipped with a thin needle.[1] The resin was washed by suspending it in DCM (1 ml) and removing the solvent after 1 hour, followed by drying over a gentle flow of argon. The resin was suspended in DCM (1 ml), except when in situ prepared catalysts were used, followed by the addition of the substrate and *n*-decane, as internal standard for GC measurements, via a freshly prepared stock-solution (total volume = 1.5 ml). The reaction vials were placed in an autoclave and the autoclave was purged three times with hydrogen (2–3 bar) and subsequently charged with 5 bar hydrogen. After 20 hours, the pressure was released and the reaction mixtures were diluted with DCM and filtered over a plug of silica to remove catalyst residues. For the experiments conducted with methyl-2-acetamidoacrylate the reaction mixture was filtered over a plug of celite, since (partial) retention of the product (and substrate) was observed with silica or neutral alumina. The yield[2] and enantiomeric excess were determined by chiral-phase capillary gas chromatography on a Trace GC Ultra (thermo electron) equipped with a BetaDex-325 column (Supelco, 30 m X 0.25 mm X 0.25 µm), applying the following GC-conditions:

– For the hydrogenation of dimethyl itaconate (**7**): 70°C (isotherm), 0.9 ml/min. (He). t_R (*R*–product) = 41.1 min.; t_R (*S*– product) = 42.0 min.; t_R (substrate) = 58.5 min.

– For the hydrogenation of methyl 2-acetamidoacrylate (**8**): 70°C (isotherm for 5 min.); 1°C/min. to 90°C; 5°C/min to 120°C (isotherm for 3 min.), 15°C/min. to 200°C (isotherm for 1 min.); 90 kPa (He). t_R (substrate) =31.2 min.; t_R (*S*–product) = 32.6 min.; t_R (*R*–product) = 33.1 min.

Catalytic performance for various homo- and hetero-ligand combinations in the rhodium-catalyzed hydrogenation of 7 or 8.

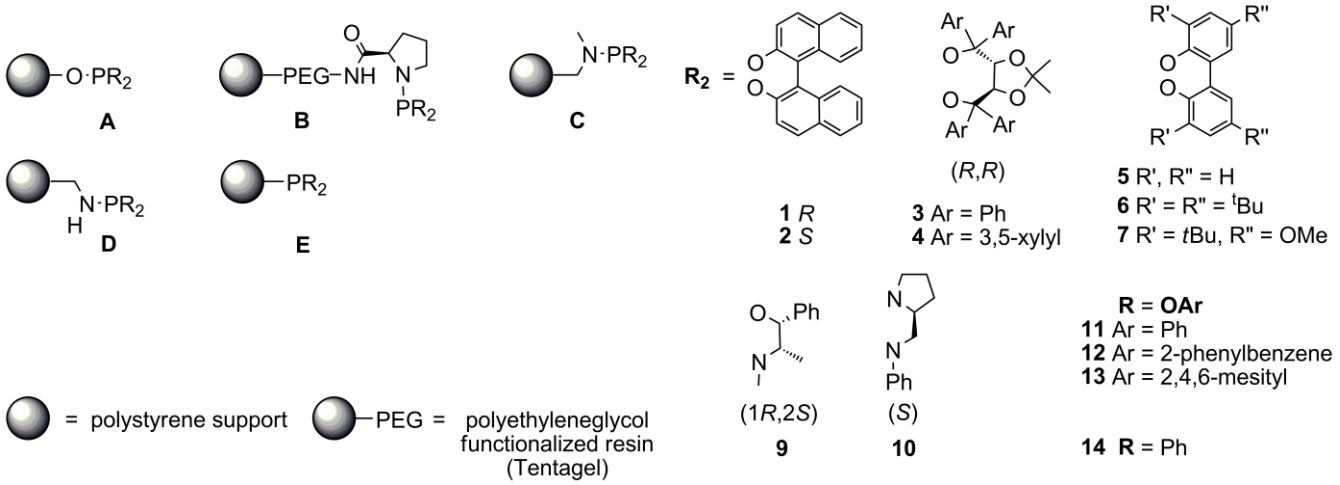


Chart 1: Structures of the supported monodentate ligands.

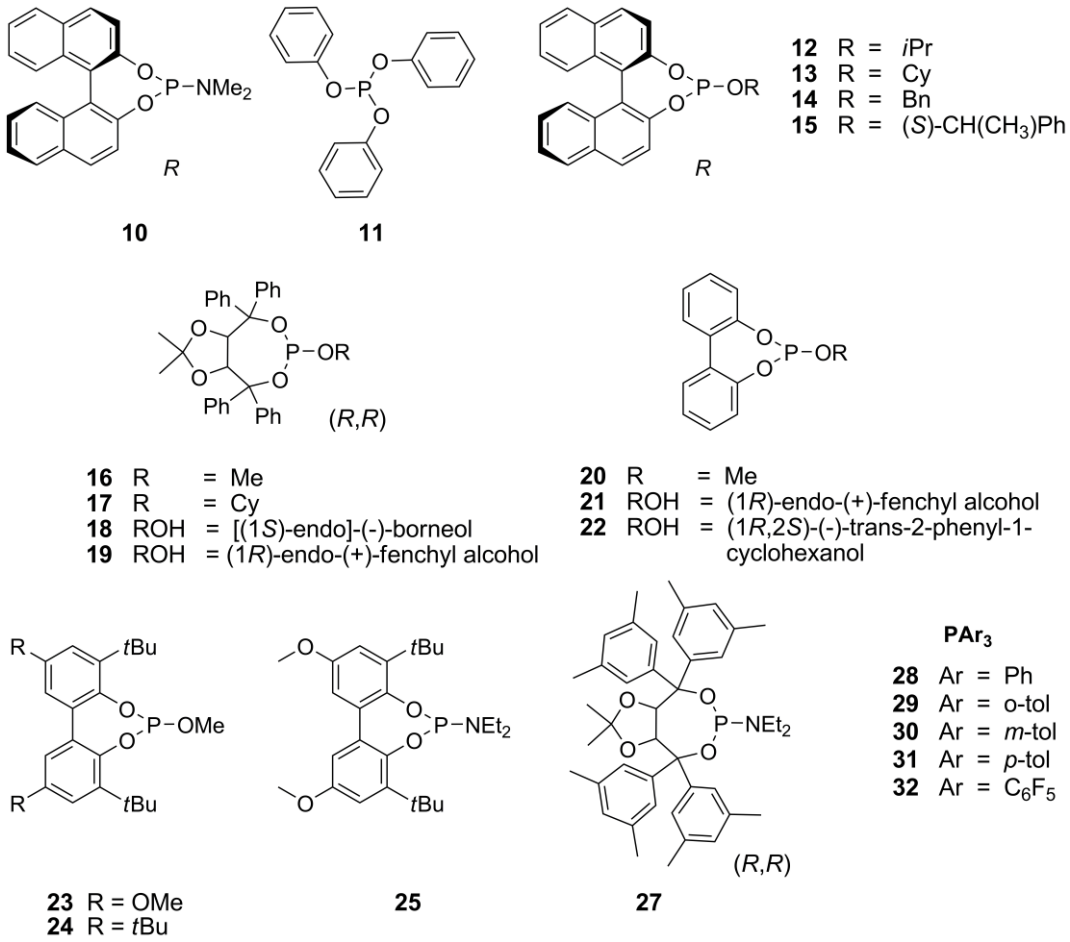


Chart 2: structures of the non-supported monodentate ligands. *Note that in the main text a different numbering is applicable.*

Table S1. Catalytic performance of in situ generated homo- and hetero-ligand combinations of **C1** in the hydrogenation of **7**.

Entry	P_a	P_b	Conversion (%)[a]	ee (%)[b]
1	**C1**	**C1**	100	70 (*R*)
2	**C1**	-	100	77 (*R*)
3	**C1**	**12**	100	93 (*R*)
4	**C1**	**13**	100	> 97 (*R*)
5	**C1**	**14**	100	91 (*R*)
6	**C1**	**15**	61	52 (*R*)
7	**C1**	**16**	100	36 (*S*)
8	**C1**	**17**	76	16 (*R*)[c]
9	**C1**	**18**	100	1 (*R*)
10	**C1**	**19**	100	57 (*S*)
11	**C1**	**20**	100	25 (*R*)
12	**C1**	**21**	100	51 (*S*)
13	**C1**	**22**	100	32 (*R*)
14	**C1**	**23**	100	30 (*R*)
15	**C1**	**24**	100	22 (*R*)
16	**12**	**12**	100	> 97 (*R*)
17	**13**	**13**	100	> 97 (*R*)
18	**16**	**16**	100	45 (*S*)
19	**17**	**17**	100	20 (*R*)
20	**18**	**18**	100	19 (*R*)
21	**19**	**19**	100	57 (*S*)
22	**21**	**21**	100	60 (*S*)

Reaction conditions: Rh/**7** 1:20, [Rh] = 5.0 mM, 5 bar H_2, CH_2Cl_2, RT. Catalyst precursor = $[Rh(COD)_2]BF_4$, catalyst incubation time is 30 minutes. Reaction time = 20 hours. [a] Based on conversion of **7**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [c] Rh/**7** 1:40, [Rh] = 2.8 mM. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$. *Note that in the main text a different numbering is applicable for the non-supported ligands.*

Table S2. Catalytic performance of in situ generated hetero-ligand combinations of supported and non-supported monodentate ligands in the hydrogenation of **7**.

Entry	Pa	Pb	Conversion (%)[a]	ee (%)[b]
1	**A2**	**25**	10	3 (*S*)
2	**A3**	**25**	38	9 (*R*)
3	**A3**	**29**	45	36 (*R*)
4	**A3**	**29**	14	25 (*R*)[c]
5	**A9**	**29**	80	40 (*R*)
6	**A10**	**29**	100	0[d]
7	**A10**	**29**	40	0[d,e]
8	**B1**	**25**	60	53 (*R*)
9	**B1**	**29**	86	46 (*S*)[c]
10	**B1**	**32**	100	38 (*S*)[c]
11	**C2**	**11**	55	32 (*S*)
12	**C2**	**25**	25	5 (*R*)
14	**C2**	**29**	9	9 (*S*)[c]
15	**C2**	**30**	50	43 (*S*)[c]
16	**C2**	**31**	88	1 (*R*)[c]
17	**C2**	**32**	47	38 (*S*)[c]

18	**E14**	**27**	18	1 (*S*)
19	-	**25**	100	0
21	**28**	**27**	68	2 (*R*)
22	**27**	**27**	0	-

Reaction conditions: Rh/**7** 1:40, [Rh] = 2.8 mM, 5 bar H_2, CH_2Cl_2, RT. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$, catalyst incubation time is 30 minutes. Reaction time = 20 hours. [a] Based on conversion of **7**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [c] Reaction mixture was not stirred. [d] Catalyst pre-formed (18 hours). Reaction time = 22 hours. [e] In toluene. *Note that in the main text a different numbering is applicable for non-supported ligands.*

Table S3. Catalytic performance of in situ generated hetero-ligand combinations of (*R*)-monophos (**10**) and polymer-supported monodentate ligands in the hydrogenation of **7**.

Entry	P_a	P_b	Conversion (%)[a]	ee (%)[b]
1	-	**10**	100	> 97 (*R*)
2	**10**	**10**	100	> 97 (*R*)
3	**A2**	**10**	100	> 97 (*R*)
4	**A2** (4 equiv.)	**10**	35	> 97 (*R*)[c]
5	**A3**	**10**	100	78 (*R*)
6	**A5**	**10**	74	> 97 (*R*)
7	**A11**	**10**	100	> 97 (*R*)
8	**A12**	**10**	67	> 97 (*R*)
9	**A13**	**10**	69	> 97 (*R*)
10	**A14**	**10**	100	71 (*R*)
11	**B1**	**10**	100	12 (*R*)
12	**C2**	**10**	70	> 97 (*R*)
13	**C5**	**10**	100	> 97 (*R*)
14	**E14**	**10**	100	73 (*R*)
15	**13**	**10**	100	73 (*R*)
16	**17**	**10**	100	46 (*R*)
17	**25**	**10**	100	> 97 (*R*)
18	**28**	**10**	100	> 97 (*R*)

Reaction conditions: Rh/**7** 1:40, [Rh] = 2.8 mM, 5 bar H_2, CH_2Cl_2, RT. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$, catalyst incubation time is 30 minutes. Reaction time = 20 hours. [a] Based on conversion of **7**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [c] Rh/ligand 1:5. *Note that in the main text a different numbering is applicable for the non-supported ligands.*

Table S4. Catalytic performance of the solution and polymeric phase of in situ generated heterocombinations in the hydrogenation of **7**.

Entry	P_a	P_b	phase	Conversion (%)[a]	ee %[b]
1	**A2**	**10**	both	100	> 97 (*R*)
2	**A2**	**10**	resin	100	5 (*R*)[c]
3	**A2**	**10**	solution	100	67 (*R*)[c]
4	**C1**	**17**	both	76	16 (*R*)
5	**C1**	**17**	resin	64	47 (*R*)[c]
6	**C1**	**17**	solution	40	13 (*R*)[c]
7	**A12**	**10**	both	21	> 97 (*R*)[d]
8	**A12**	**10**	both	67	> 97 (*R*)
9	**A12**	**10**	solution	100	> 97 (*R*)[e]
10	**A5**	**10**	both	74	> 97 (*R*)
11	**A5**	**10**	solution	100	77 (*R*)[e]
12	**E14**	**10**	both	100	73 (*R*)
13	**E14**	**10**	solution	100	> 97 (*R*)[e]

Reaction conditions: Rh/**7** 1:40, [Rh] = 2.8 mM, 5 bar H_2, CH_2Cl_2, RT. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$, catalyst incubation time is 30 minutes. Reaction time = 20 hours. [a] Based on conversion of **7**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [c] Solution and resin phase separated prior to catalysis after incubation time of 14 hours. [d] After 40 minutes reaction time. [e] Solution and resin separated

after 40 minutes reaction time. Solution phase returned to autoclave for additional 19 hours. *Note that in the main text a different numbering is applicable for the non-supported ligands.*

Table S5. Recycling of purified polymer-supported **A14**/**10** based catalysts in the hydrogenation of **7**.

Entry	P_a	P_b	Equivalents P_b	Run	Conversion (%)[a]	ee (%)[b]
1	**A14**	**10**	1	1	58	43 (*R*)[c]
2	**A14**	**10**	1	2	7	8 (*R*)[d]
3	**A14**	**10**	1	3	2	3 (*R*)[e]
4	**A14**	**10**	2	1	96	70 (*R*)[c]
5	**A14**	**10**	2	2	55	56 (*R*)[d]
6	**A14**	**10**	2	3	12	12 (*R*)[e]

Reaction conditions: ligand/**7** 1:67, [Rh] = 6.0 mM, 5 bar H_2, CH_2Cl_2, RT. Catalyst allowed to form in DCM for 16 hours, $Rh/P_a/P_b$ 1:1:1. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$. Catalyst purified by removal of the solution phase and washing of the resin twice with DCM (1.5 ml). Reaction time = 23.5 hours. [a] Based on conversion of **7**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [d] Reaction time = 22.5 hours. Resin not washed between run 1 and 2. [e] Ligand/ substrate 1:44. Reaction time = 20.5 hours. Note that in *the main text a different numbering is applicable for the non-supported ligands.*

Table S6. Catalytic performance of purified polymer-supported catalysts in the hydrogenation of **8**.

entry	P_a	P_b	Run	Conversion (%)[a]	ee (%)[b]
1	**-**	**10**	-	100	> 97 (*S*)
2	**A1**	**-**	-	100	78 (*S*)[c]
3	**A1**	**10**	-	100	88 (*S*)[d]
4	**A2**	**10**	-	100	2 (*S*)[d]
5	**A3**	**-**	-	100	5 (*R*)[c]
6	**A3**	**10**	-	100	52 (*S*)[d]
7	**A5**	**10**	-	100	33 (*S*)[d]
8	**A12**	**10**	-	100	87 (*S*)[d]
9	**A13**	**10**	-	100	64 (*S*)[d]
10	**A14**	**10**	-	100	24 (*S*)[d]
11	**C2**	-	1	96	80 (*R*)[e]
12	**C2**	-	2	13	72 (*R*)[f]
13	**C2**	**28**	1	90	3 (*R*)[e]
14	**C2**	**28**	2	11	16 (*R*)[f]
15	**C2**	**10**	1	84	48 (*R*)[e]
16	**C2**	**10**	2	5	19 (*R*)[f[
17	**E14**	-	-	100	0[g]
18	**E14**	**10**	1	100	14 (*S*)[g]
19	**E14**	**10**	2	100	4 (*S*)[g]
20	**28**	**10**	-	100	64 (*S*)[h]

Reaction conditions: Ligand/**8** 1:62, [Rh] = 1.3 mM, 5 bar H_2, CH_2Cl_2, RT. Supported catalyst allowed to form in DCM for 24 hours, $Rh/P_a/P_b$ 1:1:1. Catalyst precursor = $[(COD)Rh(MeCN)_2]BF_4$. Catalyst purified by removal of the solution phase and washing of the resin twice with DCM (1.2 ml). Reaction time = 24 hours. [a] Based on conversion of **8**, determined by GC with *n*-decane as internal standard. [b] Determined by chiral GC (Betadex 325). [c] [Rh] = 8.8 mM. [d] Ligand/**8** 1:52, [Rh] = 4.9 mM. Catalyst formed from $P_a/Rh/P_b$ 10:13:13 mixture (14 hours), washed once. Reaction time = 3 hours. [e] [Rh] = 1.3 mM. Catalyst formed from $Rh/P_a/P_b$ 100:105:100 mixture, washed once. [f] Resin washed with 1 ml DCM between run 1 en 2. Ligand/substrate 1:18. [g] Rh] = 13.7 mM. Catalyst formed from $Rh/P_a/P_b$ 100:105:100 mixture. Similar results were obtained with [Rh] = 8.8 mM and 75 minutes reaction time. [h] Taken from reference 3. *Note that in the main text a different numbering is applicable for the non-supported ligands.*

[1] It could not be prevented that small amounts of the resin were removed from the vial.
[2] Experiments were conducted to confirm that the presence of the resins does not alter the decane/substrate and decane/product ratios in the solution phase.
[3] Reetz, M.; Mehler, G. *Tetrahedron Lett.* **2003**, *44*, 4593–4596.